

**Local temporal variability in physical activity may be more important for episodic pain trajectory classification than patient-reported outcomes and summary measures of activity: implications for objective patient tracking**

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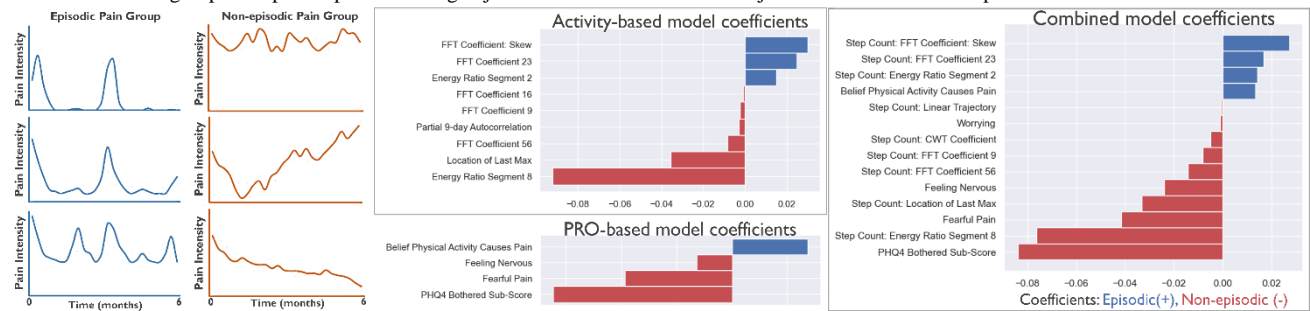
**INTRODUCTION:** Physical activity has a complex association with the patient pain experience, particularly in chronic low back pain (cLBP), where the cyclic interplay of biopsychosocial factors complicates the relationship. While physical activity can play a protective interventional role, changes in activity may be the result, rather than the driver, of fluctuations in pain and pain cognitions. Tracking fluctuations in pain and pain trajectory relies on exhaustive self-reported surveying, which is subjective in nature and clouded by the unreliability of patient recall of pain. In recent study, day-to-day variability in activity has been shown to be associated with self-reported flare-ups in cLBP, suggesting that objective, longitudinal measures of activity may be a valuable biomarker of patient pain trajectories. We hypothesized that objective measures of step count and step count variability over time would outperform patient-reported outcomes (PROs) in classifying episodic vs. non-episodic cLBP groups determined through self-reported surveying. Further, we hypothesized that local variability in physical activity (e.g., day-to-day, week-to-week variability) would be more predictive of episodic pain compared to global measures (e.g., avg daily step count). To investigate this, we extracted temporal features from six-months of daily step count data, along with comprehensive self-reported psychosocial, pain, and demographic measures from a cLBP cohort to build a series of logistic regression models predicting episodic pain trajectory classes (episodic vs non-episodic pain groups). We compared prediction performance of activity features alone to that of PROs alone, as well as prediction performance of the combined activity and PRO dataset. Further, using regularization, we identified the activity features and PROs most predictive of episodic pain trajectory.

**METHODS:** With IRB approval and informed consent, we retrospectively collected six months of step count data, measured by the iPhone HealthKit, on a cLBP patient cohort. Patients were excluded if they had more than 60 days of missing data, resulting in a final cohort of 238 patients. At the end of the six-month activity tracking period, patients completed a comprehensive survey of pain, psychosocial, and demographic questionnaires, including the Visual Trajectories Questionnaire-Pain (VTQ-Pain), a single question prompting patients to select the visual pain trajectory which best describes the course of their pain in the past 6 months (Fig. 1). Patients were binned into either ‘episodic’ or ‘non-episodic’ pain groups based on their response to VTQ-Pain. From the activity data, we extracted the daily step count time-series data for each patient for the six-month period leading up to the administration of the survey, ensuring that activity data matched the six-month period described in the VTQ-Pain questionnaire. We then used functional principal component analysis (fPCA) to identify the underlying eigenfunctions in the step count dataset, describing global trends. For each step count time-series, we also calculated an additional 615 generalized time features commonly used in time-series data analysis using the tsfresh feature extraction python library. Using the activity features as predictors, we built a logistic regression model with elastic net regularization and 3-fold cross-validation with 25 repeats to predict the pain trajectory classification. Similarly, we built logistic regression models using the PROs alone as predictors, or the combination of activity features and PROs as predictors. For each model, we calculated the mean and standard deviation of the prediction accuracy on the training data set using the best models across folds. The final model performance was scored using the prediction accuracy on the testing data set. We used a student t-test to identify differences in training accuracy between models. Further, we calculated the area under the curve (AUC) of the receiver-operating curve to measure model performance.

**RESULTS:** Of 238 patients enrolled, 77.3% were classified as having an ‘episodic’ pain trajectory, with the rest classified as ‘non-episodic’. There were no age or sex differences between groups. The fPCA identified four components representing 99% of the variation in the data. Training accuracy did not differ between the activity-based model (73.4%±5.7%) and the PRO-based model (74%±3.9%), but the test accuracy of the activity-based model (66.7%) outperformed the PRO-based model (59.7%) by 7% points. The training accuracy of the combined model did not differ from the activity-based model but was 3.5% points lower (70.5%±4.8%; pval < .01) than the PRO-based model. However, the test accuracy of the PRO-based model and the combined model were identical. Further, the activity-based model had an AUC score of .67 - higher than the PRO-based model (.58) and the combined model (.57). The activity features with the largest coefficients (importance) were measures of frequency (fast Fourier transform (FFT) coefficients), energy and variability of the step count trajectories at shorter time scales (9-day autocorrelation). The most important PROs were related to pain during physical activity and fear of pain (Fig.1)

**DISCUSSION:** We built predictive models of episodic pain trajectory classification from daily physical activity data and PROs alone. While overall model performance was low across models, the activity-based model performed at or above the level of the PRO-based model. This is an interesting finding given the sparsity of information included in the activity data, suggesting that variations in step count data alone may be more informative of patient episodic pain over time than self-reported metrics of pain and pain cognitions in later time assessments. Low model performance may be related to the subjectivity of the VTQ-Pain, and the unreliability of past recall of pain experience, rather than a lack of prediction power in the activity features. This further emphasizes the importance of objective measures, like physical activity metrics, for patient pain tracking and classification. Further, the activity features selected by the elastic net regularization were related to measures of frequency and ‘local’ variability in the step count trajectory, rather than summary measures of physical activity, like average daily step count, which is currently the physical activity measure most reported in the literature. This suggests that changes in physical activity trajectories across short time scales, like days or weeks, may be a better biomarker of patient pain experience than overall summary measures. Past study of physical activity in chronic pain patients relying only on summary measures of activity may be missing important associations between activity and pain, particularly in the temporal variations in activity and pain trajectories. Interestingly, the features selected by regularization in the PRO-based model included surveying on pain cognitions during physical activity, further suggesting an important association between pain trajectories and physical activity trajectories.

**SIGNIFICANCE:** This study suggests that activity tracking may provide an opportunity for objective monitoring of patient pain, fluctuations in pain, and improvements or response to interventions. Further, this study establishes the importance of ‘local’ measures of variability in physical activity trajectories, rather than summary measures of activity, as a possible objective surrogate for subjective self-reported measures of pain experience. Further study will look to incorporate more comprehensive activity tracking like measures of walking speed and stride length, and other metrics derivable from wearable sensors to further explore associations between trajectories of physical activity and contemporary pain. This has important implications for the development of reliable, continuous monitoring of patient pain experience using objective measures rather than subjective and discrete self-reported metrics.



**Figure 1: Model features represent ‘local’ variability in activity and maladaptive pain cognitions.** A. Depicts the visual trajectories from the VTQ-Pain classified as ‘episodic’ (blue) or ‘non-episodic’ (red). B. Model features and coefficients; ‘Episodic’: (+)in blue and ‘Non-episodic’: (-) in red